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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,847	03/30/2001	Peter J. Sims	26336-23	7002

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,847	SIMS ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Sequence Compliance

The specification remains objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific amino acid sequences comprising four or more amino acids and ten or more nucleic acids in the specification. A specific example within the specification that does not comply with the sequence rules is found Table 1 on page 56, which lists exon and intron sequences without a SEQ ID NO. Applicant is required to append a SEQ ID NO. to any sequence applicable to the rule. See 37 CFR § 1.821 (a)-(d) and MPEP § 2422.

Applicant states that the specification is being reviewed and that appropriate amendments will be provided. Until such time the amendments are received, the objection will be maintained for reasons of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record.

Applicant states that the preamble of the claims has been changed to obviate issues in the rejections concerning infection and appropriate animal models.

The amended preamble has been considered, but does not obviate or circumvent issues in the rejection concerning viral infectivity and appropriate animal models. The claims are currently drawn to a method of inhibiting or preventing viral budding. This method is not limited to *in vitro* inhibition, but also encompasses preventing viral budding *in vivo*. In addition, it is clearly evident that the nature of the invention is to prevent viral infection by introducing a phospholipid scramblase polypeptide into cells (*in vitro* or *in vivo*), see paragraph 21 of the disclosure and originally presented claims 26-34 for example.

Applicant also states that the results of Example 4 indicates that phospholipid scramblase cooperates with other INF-induced proteins to inhibit VSV infection. Applicant also points to paragraph 138, which states that cells expressing enzyme cDNA had a viability of 33% compared to the 7% viability of control cells. Applicant asserts that the data conclude that expression of PLSCR1 results in a significant reduction in the cytopathic effect of VSV infection and that the results clearly show an inhibition or reduction of the disease state of the cell line and that there is no adverse effect on routine cellular function.

Applicant's arguments and a review of Example 4 have been fully considered, but are found unpersuasive. Due to the fact that VSV replication is highly susceptible to INF (see paragraph 137 of the disclosure), it is maintained that it cannot be readily determined if the presence of PLSCR1 or INF is responsible for the 25-fold enhancement of INF anti-VSV infection for infected cells since both substances are present in the working example (see paragraph 139). While the 33% viability of cells expressing PLSCR1 in paragraph 138 applicant

cites is encouraging, this data does not indicate that there is inhibition or prevention of virus budding, which is a required element of the claims. It is noted that the results indicate that there is only a slight reduction of viral yield with the enzyme alone. Applicant's assertion that there is no adverse effect on routine cellular function is only speculative since there is no data presented which measures adverse effects of the cells.

Applicant also argues that the presence of the motif PPxY enables the inhibition of viral budding and the targeted motif, WW, is well characterized so that the ordinary artisan would be able to recognize peptides having the required activity.

In response, it is maintained that the skilled artisan would be unable to make the scope of the claimed genus because the species are unrecognizable in view of the fact that the structural motif does not correlate with a recognized function. Therefore, the skilled artisan would be unable to determine whether a fragment containing the motif would have the required function because the function is not clearly defined by the inventors or the art, see page 3 page 12, paragraph 50, and page 63, paragraph 177 of the specification and the teachings of Sims et al. (Thrombosis and Haemostasis. 2001; 86 (1): 266-275, abstract only). The disclosure states that the presumed activity of phospholipid scramblase on cell membranes cannot be predicted by level of enzyme expression, but that other factors are involved. However, there is no teaching or indication that would enable one skilled in the art consider what these other unknown factors alluded to are. While it is within the skill of the artisan to make PPxY motifs in peptides, it is beyond the skill of the artisan to confirm the functionality of the peptide fragments because the function of the parent is ambiguous. There is no clear example of viral inhibition in the

disclosure with the full parental sequence or with any peptide fragment containing the PPxY motif.

The skilled artisan would also be unable to predict the effect of the enzyme merely by accomplishing its expression in a recombinant cell in vitro because the disclosure fails to teach effective delivery of Phospholipid Scramblase containing the PPxY motif in effective amounts to inhibit viral infection. The skilled artisan would be concerned about delivering such an enzyme or fragments thereof to cells because Phospholipid Scramblase function has not been clearly defined, see Sims et al. *supra*. There is also no teaching in the specification that addresses concerns in the art for effective delivery while not interrupting normal cellular function. There is no way to determine how the instant enzyme, delivered in such large quantities in order to bind every protein comprising a WW motif would effect the host. This concern is also admitted in the specification at the top of page 64.

The claims encompass preventing viral infection in known viruses such as Ebola, Marburg, and HIV, with no art-recognized animal model. See the reviews of Wilson et al. (Cellular and Molecular Life Sciences. 2001; 58 (12-13): 1826-41) and Klein et al. (Clinical Therapeutics. 2000; 22 (3): 295-314) for general teaching in the art for HIV and Ebola vaccines. The specification does not teach an appropriate animal model for these viruses or use an animal model for other viruses to be inhibited.

For these reasons, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make and/or use the invention.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 10:00 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Primary Examiner
Art Unit 1648